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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,549	10/29/2001	Michael A. Bowen	D0034 NP	8020

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	9

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,549	BOWEN ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *6-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's election without traverse of Group I, Claims 1-5 and 18 in Paper No. 8 is acknowledged.

Claims 6-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 8.

Claims 1-5 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (upon which Claims 2-5 and 18 depend) is indefinite in the recitation of "ubiquitin conjugating enzyme homologue" as it is unclear if the encoded protein must have ubiquitin conjugating activity or merely have "homology" to a ubiquitin conjugating enzyme. Furthermore, if the claim terminology does not require the encoded protein to have ubiquitin conjugating activity it is unclear what features a "homologue" must have.

Claim 1 parts (e) or (f) are confusing as part (e) recites "nucleotides 517-1782 of SEQ ID NO:1 wherein said nucleotides encode a polypeptide of SEQ ID NO:2 **minus** the start codon" and part (f) recites "nucleotides 520-1782 of SEQ ID NO:1 wherein said nucleotides encode a polypeptide of SEQ ID NO:2 **including**

the start codon" however nucleotides 517-519 of SEQ ID NO:1 are the nucleotides encoding the start codon of SEQ ID NO:2. As such it appears part (e) should recite "**including** the start codon" and part (f) "**minus** the start codon".

Claims 1-5 and 18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The applicant has asserted utility for the polypeptide of SEQ ID NO:2 encoded by the claimed isolated polynucleotide of SEQ ID NO:1 as a ubiquitin conjugating enzyme or for "diagnosis, treatment or prevention of cancers and tumors, or immune, lymphoproliferative, or neurodegenerative disorders". However, the asserted utilities are not specific and substantial. While the specification includes sufficient evidence for the skilled artisan to believe that the protein of SEQ ID NO:2 is a ubiquitin conjugating enzyme, the specification fails to assert what protein(s), SEQ ID NO:5 conjugates ubiquitin to. Ubiquitin conjugating enzymes comprise a highly diverse group of proteins which conjugate ubiquitin to a wide variety of different proteins with different enzymes having an enormous diversity in the specificity of substrates utilized (See for example Hershko et al). As ubiquitin conjugating enzymes are such a large diverse

family of enzymes, a mere disclosure that a protein is a ubiquitin conjugating enzyme without a more specific recitation of what type of ubiquitin conjugating enzyme (i.e., what protein(s) is/are conjugated) is insufficient to provide a substantial utility as the skilled artisan would require further research to identify or reasonably confirm a real world context of use. The specification also lists a general use for the polypeptides encoded by the claimed polynucleotides as useful for "diagnosis, treatment or prevention of cancers and tumors, or immune, lymphoproliferative, or neurodegenerative disorders". However, there is no information that links the use of the polypeptide of SEQ ID NO:2 or the polynucleotide of SEQ ID NO:1 and its variants to any specific disease state. Thus the asserted utility of the claimed polynucleotides and its variants is not substantial or specific. Further, while the specification discloses that SEQ ID NO:1 and its fragments will be used to generate probes, that is not a utility specific to the claimed polynucleotide sequence. For all the reasons detailed above, the claimed polynucleotides lack, a specific, substantial and credible utility

Claims 1-5 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of DNA molecules encoding any ubiquitin conjugating enzyme in view of the recitation in Claim 1, part (a) of ubiquitin conjugating enzymes comprising any fragment of SEQ ID NO:2, as all ubiquitin conjugating enzymes will comprise at least one or more amino acids present in SEQ ID NO:2. The specification teaches the structure of only a single representative species of such DNAs i.e., SEQ ID NO:1. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding a ubiquitin conjugating enzyme. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-5 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding SEQ ID NO:2, does not reasonably provide enablement for any polynucleotide encoding any ubiquitin conjugating enzyme comprising a fragment of SEQ ID NO:2. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-5 and 18 are so broad as to encompass any polynucleotide encoding any ubiquitin conjugating enzyme. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a single ubiquitin conjugating enzyme and its encoding polynucleotide.

While recombinant and mutagenesis techniques are known, it is <u>not</u> routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid

modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all polynucleotides encoding any ubiquitin conjugating enzyme because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting ubiquitin conjugating activity; (B) the general tolerance of ubiquitin conjugating enzymes to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any ubiquitin conjugating enzyme residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the

scope of the claims broadly including any polynucleotide encoding any ubiquitin conjugating enzyme. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-5 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel organisms. Since the organisms are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed organisms sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the

organisms. The specification does not disclose a repeatable process to obtain the organisms and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these organisms should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
4. the deposit will be replaced if it should ever become inviable.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country,

> more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Specht et al. (WO99/46375).

Specht et al. teach a nucleic acid (SEQ ID NO:217 of Specht et al.), expression vectors and host cells comprising this nucleic acid and use of this nucleic acid as a probe to isolate nucleic acids which hybridize therewith. (See the enclosed Derwent Abstract). SEQ ID NO:217 of Specht et al. is identical to residues 587-2251 of SEQ ID NO:1 of the instant application with the exception of the insertion of a G following residue 671 and a single mismatch at residue 2239. As the nucleic acid of Specht et al. includes all of the sequence encoding the catalytic domain (i.e., residues 248-411) of SEQ ID NO:2, this nucleic acid also encodes a ubiquitin conjugating enzyme.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant

is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Specht et al. (WO 99/46375).

Specht et al. is discussed above.

As Specht et al. teach that a use of the disclosed nucleic acids is as a probe to isolate nucleic acids which hybridize therewith, it would have been obvious to one of ordinary skill to make a kit containing all the components necessary for the detection of such nucleic acids by a hybridization assay (i.e., the probe, instructions and optionally reagents for detection of hybridization).

The references AM, AS, AT, AA, AB and AC of the information disclosure statement filed 7-16-02 have not been considered as they fails to comply with 37 CFR 1.98. The IDS does not contain a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of reference AM which is not in the English language and the PTO-1449 listing of references AS, AT, AA, AB and AC fails to provide proper citations.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652